

Attorney Docket No. 9286.7
Application Serial No.: 10/019,902
Filed: July 2, 2002

REMARKS

Claims 1-6, 8-12, 14-16, 18, 20, 23, 27 and 28 are pending in this application. Claims 1, 10, 12, 15, 18, 23, 27 and 28 are amended herein for clarity to more particularly define the invention. Support for these amendments is found throughout the specification and in the language of the original claims, as set forth below. No new matter is added by these amendments and their entry and consideration is respectfully requested. In light of these amendments and the following remarks, applicants respectfully request reconsideration of this application and allowance of the pending claims to issue.

I. Request for withdrawal of improper final rejection

The present Office Action is stated to be a final Office Action. It is noted that on page 6 of the Office Action it is also stated that "[a]pplicants' argument necessitated the new ground of rejection presented in this Office Action." Applicants note that the new ground of rejection in the present Office Action is the rejection of claims 1-6, 8, 18 and 23 on the basis that such claims are allegedly anticipated by PCT publication no. WO 98/14215, which is a reference that was not previously of record in this application.

It is stated in the MPEP under section 706.07(a), that "[u]nder present practice, second or any subsequent actions on the merits shall be final, except where the examiner introduces a new ground of rejection that is neither necessitated by applicant's amendment of the claims nor based on information submitted in an information disclosure statement filed during the period set forth in 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.117(p)." (emphasis added).

Applicants respectfully point out that there is no basis in the MPEP for a new ground of rejection in a final Office Action based only on applicants' arguments and not on applicants' amendments to the claims. In fact, it is stated in the MPEP in this section that the Examiner is to use Form Paragraph 7.40, entitled "Action Is Final, Necessitated by Amendment," which reads as follows: Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP 706.07(a).

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Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a)." The Examiner appears to have modified Form Paragraph 7.40 to replace the term "amendment" with the term "argument." This modified version of Form Paragraph 7.40 is not found anywhere in the MPEP nor does the MPEP describe a situation where applicants' arguments can be the basis for a new ground of rejection in a final Office Action.

Furthermore, even if it could be argued that applicants' amendments to the claims as introduced on January 10, 2005 could be the basis for a new ground of rejection in a final Office Action, applicants point out that the only amendment to the claims made in the January 10, 2005 Amendment was the addition of the phrase " A^2 - A^3 can be any A^2 and any A^3 in any combination." It would be readily apparent to one of ordinary skill in the art that the addition of this phrase would not change the interpretation of these claims in an evaluation of whether PCT publication no. WO 98/14215 was anticipatory. In other words, if a 35 U.S.C. § 102(b) rejection of claims 1-6, 8, 18 and 23 was deemed to be necessary by the Examiner in the present final Office Action, then such a rejection should have been deemed to be necessary in the September 10, 2004 nonfinal Office Action. Thus, applicants' amendments to the claims in the January 10, 2005 Amendment did not necessitate the new ground of rejection in the current final Office Action.

In addition, applicants point out that the argument upon which the Examiner is basing the necessity for a new ground of rejection is an argument that the Examiner has decided to interpret in a manner that is not supported by any other evidence in the application. In particular, the Examiner states that because applicants argued that "association may and can take place under other conditions that can be determined by routine experimentation," it is her assumption that it must be applicants' position that "...proviso (3) of claim 1 is not actually limiting." (Office Action, page 3, first paragraph). The Examiner presents no evidence to support this interpretation of applicants' position other than her own personal opinion and such an interpretation is contradictory to applicants' arguments and to the reading of the claims. In particular, if it was indeed applicants' position that proviso (3) of claim 1 was not intended to be a limitation, then applicants would have removed it from claim 1. Thus, the Examiner's

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interpretation is inconsistent and incorrect and is not a proper basis for a new ground of rejection in a final Office Action.

Thus, for the reasons presented above, the finality of the present Office Action is improper and its withdrawal is respectfully requested. Should the finality of this Action be maintained, applicants respectfully request a written statement of explanation not only from the Examiner, but also from the Examiner's supervisor, Mr. James O. Wilson, with citation to the MPEP section that supports a final Office Action under these circumstances.

II. Rejection under 35 U.S.C. § 112, first paragraph

The Office Action states that claims 1-6, 8-12, 14-16, 18, 20, 23, 27 and 28 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly lacking enablement. Specifically, the Office Action states that the specification, while being enabling for the examples disclosed in the specification that are described as forming aggregates and having utility in the inhibition of the influenza virus, allegedly does not reasonably provide enablement for the full scope of compounds embraced by the formula wherein $X=CH_{4-m}$.

As noted above, the Examiner addresses the applicants' arguments submitted in the January 10, 2005 response by stating that, on the basis of applicants' statement that "association may and can take place under other conditions that can be determined by routine experimentation" that it appears to the Examiner that applicants' position is that "aggregation under *some set of conditions* is an inherent property of the compounds that are structurally consistent with the instant claims." (Office Action, page 3, first paragraph). From this assumption, the Examiner further interprets applicants' position to be that "...proviso (3) of claim 1 is not actually limiting." (Office Action, page 3, first paragraph).

Applicants respectfully point out that the Examiner has misinterpreted applicants' position as presented in the January 10, 2005 Amendment. Applicants' position then and now is that the claimed compounds can associate into aggregates under conditions that may not be

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identical for all of the claimed compounds but that can be readily determined for any of the claimed compounds by one of ordinary skill in the art according to the methods set forth in the instant specification and as would be known in the art. Thus, contrary to the Examiner's unsupported interpretation, it is not applicants' position that proviso (3) of claim 1 not be limiting.

Specifically, as set forth throughout the specification, the present invention is based on the discovery that the claimed compounds are capable of forming non-covalent aggregates, which can be used for dynamically coupling a ligand arrangement to a receptor arrangement for improved binding affinity. Thus, this proviso is included in claim 1 and other claims to define the genus of compounds of this invention, having particular X, B and m values that allow formation of aggregates. The determination of such X, B and m values for any particular compound encompassed within this claim would be readily determined by the ordinary artisan without undue experimentation, according to known methods, as demonstrated, among other places, in the Examples section of the instant application.

Thus, it is intended by applicants that compounds of this invention are those that form aggregates in accordance with the teachings of the specification and art-known methods for producing aggregates and identifying aggregate formation. In the present application, applicants have demonstrated that the compound disclosed in PCT publication WO 98/14215 does not form aggregates (see Comparison Example 1 on pp 40-41 of the instant specification). Thus, the compound of PCT publication WO 98/14215 is not included in the genus of compounds of the claimed invention.

Although the claims are adequately enabled as previously pending, in order to expedite prosecution of these claims to issue and to clarify applicants' invention, claim 1 is amended herein to recite a compound of the general formula (I)



wherein

X is an m-valent unit and

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- B are identical or different and denote K-R, wherein
- K is a bond or is $A^1-(A^2-A^3)_k-sp$, wherein
- A^1 is $(CH_2)_tY(CH_2)_u$, wherein
- Y is $>C=O$, $>NH$, $-O-$, $-S-$ or a bond,
- t is an integer from 0 to 6 and
- u is an integer from 0 to 6,
- (A^2-A^3) can be any A^2 and any A^3 in any combination,
- A^2 is $-NHCO-$ or $-CONH-$,
- A^3 is $(CH_2)_r$, $O(CH_2)_r$, or $S(CH_2)_r$, wherein
- $r = 1$,
- sp is a divalent spacer or a bond, and
- k is an integer from 5 to 100, and
- R is hydrogen or a ligand suitable for specific bonding to a receptor; and
- m is at least 2,
- with the proviso that
- (1) in the compound at least one R is not hydrogen,
 - (2) there are at least two K that are not a bond, and
 - (3) X, B and m are so selected that an intermolecular association of the K in liquid phase by the formation of hydrogen bonds is possible, with formation of aggregates that present on the surface a plurality of R that are not hydrogen, and
 - (4) the molar mass of the fragment $X(K)_m$ is less than 20,000.

Support for this amendment to claim 1 and for similar amendments to claims 10, 12, 15, 18, 23, 27, 28 is found throughout the specification and in the language of the original claims.

As amended, the instant claims encompass compounds wherein the possible combinations of A^2 and A^3 are glyceryl moieties or moieties structurally very similar to glyceryl moieties, all of which are adequately enabled according to the teachings and examples set forth in the present specification, as acknowledged in the Office Action. Moreover, group K of the claimed compounds has an inner segment having at least five glyceryl or glyceryl-like moieties and

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therefore, the inner segments of all groups K of the claimed compounds are structurally similar. Thus, the invention as claimed is adequately enabled in this regard.

Applicants further note that the claims cover a range of compounds of formula (I) wherein k varies from 5 to 100. It would be well recognized by one of ordinary skill in the art that variations in the assembling capabilities of the compounds can be influenced by properties of the medium such as pH, salt concentrations and temperature, etc., as shown, e.g., in Fig. 3; on page 13, second and third paragraphs; and in original claim 15 of the present application. Such factors that influence aggregation of the compounds of the invention are an indication that the chemical and physical properties of the compounds depend on environmental conditions, as is well understood by the ordinary artisan.

Applicants further point out that Formula (I) comprises compounds wherein k is in the range of from 5 to 100. At $k < 5$, no aggregation takes place. At $k = 5$, the aggregation capabilities of the compounds of formula (I) commence but can be weak under certain conditions. However, the second entry in Table 2 on page 15 of the specification shows inhibition of viral cell adhesion with a compound wherein $k = 5$. Thus, although the aggregation capabilities of some of the compounds of formula (I) may be weak under some conditions at the lower limit for the value of k, it is clear that the specification is still adequately enabled for the full scope of the claimed compounds having a claimed value of k.

Furthermore, it is well established in patent case law that the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984) (prophetic examples do not make the disclosure nonenabling). (See MPEP § 2164.08(b)). As explained herein, it is clear that the teachings of the instant specification and art-known protocols provide adequate guidance for one of ordinary

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skill in the art to produce and test the compounds of the claimed invention and readily identify those that are operative or inoperative without undue experimentation.

In regard to enablement of the full range of possible groups R of the claimed compounds, applicants respectfully point out that the specification and claims provide numerous examples of a group R of this invention (see e.g., pages 7-8 of the specification and original claims 7 and 8) and provide data for specific groups R in two completely different systems: 1) the inhibition of binding of influenza virus to cells (e.g., Examples 6, 10 and 13; Tables 1,2, 8 and 9); and 2) the inhibition of complement-dependent cytotoxicity (e.g., Examples 8 and 11; page 15, first paragraph). Thus, the specification as filed provides adequate teaching for one of skill in the art to produce a compound of this invention comprising any R group of this invention and test that compound for the desired inhibition according to the methods set forth in the present application and as would be well known in the art, without undue experimentation. Thus, the present invention is enabled for the groups R of this invention.

For at least the reasons set forth above, applicants have demonstrated that the claimed invention is adequately enabled and applicants respectfully request the withdrawal of this rejection and allowance of the pending claims to issue.

III. Rejection under 35 U.S.C. § 102(b)

The Office Action states that claims 1-6, 8, 18 and 23 are rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by PCT publication no. WO 98/14215 to Bovin et al. Specifically, the Office Action states that, on the basis of the Examiner's interpretation of applicants' position that proviso (3) of claim 1 is not limiting, Example 7 of Bovin et al. discloses a compound that is consistent with the structural formula of the instant claims.

As noted above, the Examiner is incorrect in this interpretation of applicants' position. As also noted above, in the present application, applicants have demonstrated that the compound disclosed in PCT publication WO 98/14215 does not form aggregates (see Comparison Example 1 on pp 40-41 of the instant specification). Thus, the compound of PCT publication WO

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98/14215 is not included in the genus of compounds of the claimed invention and the compound of Example 7 does not anticipate the claimed invention. Thus, this rejection has been rendered moot and applicants respectfully request its withdrawal.

The Examiner is encouraged and invited to contact the undersigned directly at (919) 854-1400 if such contact will expedite the prosecution of this application to allowance.

Applicants hereby authorize the Commissioner to charge Deposit Account No. 50-0220 in the amount of \$450.00 for a two month extension of time. This amount is believed to be correct. However, the Commissioner is authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220

Respectfully submitted,

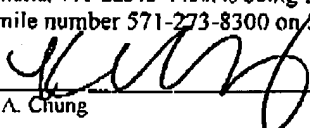


Mary L. Miller
Registration No. 39,303

USPTO Customer No. 20792
Myers Bigel Sibley & Sajovec, P.A.
Post Office Box 37428
Raleigh, NC 27627
Telephone (919) 854-1400
Facsimile (919) 854-1401

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UNDER 37 CFR 1.8**

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Katie A. Chung